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EXAMINER	
FOSTER, CHRISTINE E	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,662	VANDEKERCKHOVE ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13 and 14* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/11/05, 2/22/08* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/22/2009 has been entered.

Claims 1 and 3-7 were amended. New claims 13-14 have been added. Accordingly, claims 1-7 and 13-14 are currently pending and subject to examination below.

Objections/ Rejections Withdrawn

2. The objection to the specification is withdrawn in view of Applicant's amendments thereto and in view of the sequence listing filed on 12/22/2008.

3. The objections to claims 3 and 5-7 as set forth in the previous Office action have been withdrawn in response to Applicant's amendments.

4. The rejections under § 112, 2nd paragraph as set forth in the previous Office action have been withdrawn in response to Applicant's amendments.

5. The rejections of claims 1-2 and 4 under 35 U.S.C. 102(b) as being anticipated by Creighton have been withdrawn in response to Applicant's amendments to recite that the complex mixture of molecules contains 100 or more different molecules.

6. The rejections of claims 1 and 5 under 35 U.S.C. 102(b) as being anticipated by Cruickshank have been withdrawn in response to the above-mentioned amendments as well as

the amendments to refer to "elution time" which conveys liquid chromatography rather that the paper chromatography methods used by Cruickshank.

Claim Objections

7. Claim 1 is objected to because of the following informalities:

8. Claim 1 refers to "a target molecule or interaction partner" in part (a). While the claim refers elsewhere to a "specific interaction partner", there are no other references in the claim to a "target molecule". This presents confusion as it is unclear how the "target molecule" mentioned in part (a) fits into the rest of the method. Is a target molecule being considered the same as an "interaction partner"? Are target molecules as well as interaction partners isolated by the method? Clarification is requested.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-7 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

11. Claim 1, as amended in the instant Reply, recites step (a) in which the compound is added "to a complex mixture of molecules, containing 100 or more different molecules". Applicant argues that support for the noted limitation may be found on page 23 (see Reply of 12/22/2008 at page 8), which discloses as follows:

> The proteome will be a complex mixture of proteins, generally having at least about 20 different proteins, usually at least about 50 different proteins and in most cases 100 different proteins or more.

In now referring to a complex mixture of *molecules*, the amendments broaden beyond the scope of the original disclosure which discussed a complex mixture of *proteins* that make up the proteome.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 5 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 5 recites the limitation "the targets" in line 2. There is insufficient antecedent basis for this limitation in the claim.

15. Regarding claim 14, Applicant's meaning is not understood. First, the grammatical structure of the claim renders the meaning unclear because the claim is a run-on-sentence. Second, the claim recites that fractions are pooled in “such a way” that elution overlap is avoided. This language is vague and indefinite as it fails to make clear in what way the fractions are actually being pooled.

In addition, the claim refers to “complexes originating from different fractions”, yet the independent claim does not require or imply that complexes would originate from multiple fractions. Similarly, the claim refers to “complexes from one fraction and molecules from one or more other fractions". As best understood, this suggests that complexes and molecules are being eluted into different, non-overlapping fractions. However, the independent claim does not provide proper antecedent basis for such concepts. Rather, claim 1 states in step (b) that both complexes and molecules are present "in a fraction", implying co-elution of complexes and molecules. In addition, it is not made clear what is meant by "elution overlap" or how this term relates back to the chromatographic separation method performed in claim 1.

For the purposes of examination, the claim was interpreted as meaning that the chromatographic separation is performed so as to avoid elution of multiple overlapping peaks into the same fraction.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Creighton, T.E. ("Proteins: Structures and Molecular Properties" Second Edition, W.H. Freeman and Company, New York, 1993), pages 10-20 and 31-41) in view of Aebersold et al. (U.S. 6,670,194 B1).

Creighton teaches diagonal techniques for the purification of peptides (i.e., specific interaction partners), in which those peptides in a peptide mixture that contain a particular amino acid are selectively isolated in two electrophoretic or chromatographic steps, which are performed with an intervening step modification step that alters the mobilities of modified peptides (see page 41). Specifically, the reference teaches (a) adding a compound (e.g., iodoacetic acid, cyclohexanedione, or trifluoroacetyl, maleyl, or dinitrophenyl groups) to a complex mixture of peptides, wherein the compounds covalently modify specific amino acid residues in a peptide to form modified amino acid residues (see page 41 and also at pages 10-20 and 38-40, in particular at Equations 1.84, 1.22, 1.45, 1.79, 1.80, and 1.29).

Creighton further teaches (b) performing a first separation step, which may be performed either by electrophoresis or by the more common high-pressure liquid chromatography (HPLC) analysis (page 41, right column, the second full paragraph; and left column, the first full paragraph).

After the first separation, fractions are (c) subjected to an intervening modification so as to change the properties of the peptides which have been selectively modified by the compound.

For example, the compound maleic anhydride can be added to modify lysine-containing peptides (page 41, right column and page 11, left column including Equation 1.22). After the first separation, the compound is removed (i.e., altered). As another example, the compound cyclohexanedione can be added to selectively modify arginine-containing peptides (page 41, right column and page 12, right column including Equation 1.29). After the first separation, arginine residues are regenerated by alkaline pH treatment (i.e., the cyclohexanedione compound is removed).

When the peptides are (d) subjected to the same separation procedure a second time, peptides that have been modified by the compound will be isolated (see left column, the second full paragraph). As explained on page 41, third paragraph, when using HPLC chromatography, fractions must be modified and then reanalyzed (i.e., re-chromatographed). Similar techniques can also be performed for chemical modification of a variety of amino acids using different compounds (page 41, right column; and pages 10-10).

The compounds taught by Creighton possess the functional limitations claimed because they are capable of reacting with a functionality present in the interacting peptides. For example, cyclohexanedione as taught by Creighton is capable of reacting with the arginine-containing peptides as discussed above. Because these two moieties react in a specific manner, the chemical structure of cyclohexanedione may also be said to determine the specific interaction thereof. In addition, the compounds are altered after the first separation as discussed above. With respect to the recitation that complexes containing the altered compound elutes at a different elution time as compared to complexes containing non-altered compound, Creighton makes clear that the mobilities of peptides that have been modified after the first separation are different in the

second separation. Because the peptides have different mobilities, this is strong scientific evidence that the peptides would in fact elute at different elution times.

The teachings of Creighton differ from the instantly claimed invention in that the reference fails to specifically teach that the complex mixture of peptides to which the compound is added contains "100 or more different molecules". Creighton teaches a "mixture of peptides" but does not specify the number of different peptides in the mixture.

However, those of skill in the art at the time of the instant invention recognized the value in performing large-scale analyses of proteins in a so-called "proteomics" approach.

Aebersold et al. discuss the recognized importance of proteins in biological processes. Like large-scale genomic analysis, global analysis of proteins expressed in a cell or tissue is also essential to describe a biological system (column 1, lines 20-60). Such complex samples can be analyzed in order to identify proteins in the context of disease states (column 3, lines 8-46). Techniques to assay proteins expressed in complex samples (such as blood, cells, tissues, and fractions thereof) are therefore desirable (see column 1, line 60 to column 3, line 45). It is noted that the instant specification indicates that the proteome is a complex mixture of proteins that in most cases has 100 different proteins or more (page 23, lines 26-35). Further, it is disclosed that a proteome is present in such samples as intact cells, lysate, biological fluid, etc. (ibid). Because these same samples are taught by Aebersold et al., it is presumed that they would necessarily contain 100 different proteins or more.

In addition, Aebersold et al. also teach simultaneous “multiplex" analysis of multiple proteins or of multiple samples in a single analysis (see column 6, lines 40-45; column 7, lines

37-42). For example, sequence identification of multiple peptide components of a protein mixture can be obtained in a single analysis (see also heading to Table 2).

To accomplish this goal of assaying proteins in complex samples, Aebersold et al. set forth a basic approach to analyze and detect specific proteins in complex samples (see especially at column 2, lines 49-57). Their approach involves selectively labeling and isolating specific peptide fragments from complex mixtures, and then characterizing the isolated peptides by mass spectrometric techniques (column 3, line 39 to column 7, line 42).

Similar to the labeling of specific amino acids such as cysteine as taught by Creighton, the labeling methods of Aebersold et al. also involve the use of compounds that have specific reactivity for certain protein groups, such as for sulfhydryl groups on cysteines (see Aebersold et al. for example at column 4, lines 27-39; column 6, lines 49-59; column 10, lines 30-43; column 15, line 54 to column 16, line 24). Next, proteins in the labeled sample are cleaved into peptides, and the labeled peptides are selectively isolated using chromatography procedures (see Aebersold et al. at column 5, lines 44-51; column 7, lines 10-15). Finally, labeled peptides are characterized by mass spectrometric techniques, e.g. to determine their amino acid sequence and identify the originating protein (column 3, line 39 to column 7, line 42 and especially at column 4, lines 54-60; see also at column 12, line 62 to column 13, line 65; and at columns 36-38).

The methods of Aebersold et al. are therefore highly analogous to those of Creighton in that they involve selectively labeling certain protein groups (e.g., cysteines) and then isolating peptides that have been labeled.

Therefore, it would have been obvious to one of ordinary skill in the art to perform the diagonal chromatography techniques of Creighton on complex samples such as those taught by

Aebersold et al. In particular, Aebersold et al. teach proteome analysis on complex samples such as blood, cells, tissues, and fractions thereof. As discussed above, the instant specification indicates that such samples represent a proteome, which in most cases contains 100 different proteins or more. Since Aebersold et al. teach the same sample types as disclosed instantly, therefore, it is presumed that such samples would also contain 100 different proteins or more.

One would be motivated to apply the diagonal chromatographic techniques to the analysis of complex mixtures containing 100 different proteins or more (such as blood or cells) in order to conduct large-scale proteomic analysis, in view of the teachings of Aebersold et al. that the large-scale analysis of proteins (proteomics) is essential in order to completely describe a biological system. More generally, one would be motivated to analyze very complex samples such as blood, cells, or tissue as taught by Aebersold et al. because Aebersold et al. taught that analysis of proteomes can be used to identify proteins whose expression level is changed in response to various disease states. Therefore, one would be motivated to study complex biological samples in order to identify proteins that play a role in disease.

Notwithstanding the above, even though Aebersold et al. do not specifically teach that the complex samples analyzed contain 100 different proteins or more, absent evidence of criticality it would have been obvious to arrive at the claimed invention because the instant specification indicates that such samples as taught by Aebersold et al. will in most cases contain many different proteins. When taken together with the teachings of Aebersold et al. that the large-scale analysis of proteins expressed in a cell or tissue is important for completely describing a biological system, one would have been motivated to analyze samples containing as many

proteins as possible in order to obtain as much information as possible about a particular biological system.

One would have a reasonable expectation of success in employing the diagonal chromatography procedures of Creighton to analyze complex samples because the teachings of Aebersold et al. indicate that proteins which have been selectively labeled and isolated from complex mixtures can be successfully analyzed according to known methods, namely by mass spectrometry. Consequently, one of ordinary skill in the art would expect success in applying the methods of Creighton to analyze complex samples such as blood in conjunction with mass spectrometry analysis of the isolated, labeled peptides.

In addition, because Aebersold et al. also teach that their methods are compatible with any fractionation methods that reduce the complexity of the sample (column 16, lines 20-24), one of ordinary skill in the art would have had a reasonable expectation of success in analyzing complex mixtures fractionated by the methods of Creighton by the mass spectrometry techniques of Aebersold et al.

With respect to claim 2, Creighton teaches a "mixture of peptides" as discussed above. Aebersold et al. teaches samples such as blood, cells or tissue (i.e., complex mixtures of proteins).

With respect to claims 3-4, it is acknowledged that Creighton fails to specifically teach adding the compound to a complex protein mixture that is then *cleaved* into a protein peptide mixture prior to separation step (b). Rather, in Creighton the compound is added to a protein peptide mixture; there is no specific teaching of a step in which the peptides are initially obtained by cleavage of proteins.

However, Aebersold et al. also teaches digesting labeled protein samples with proteases to produce peptide fragments prior to analysis by mass spectrometry (column 3, lines 39-68; column 5, lines 33-60; column 12, lines 44-53). In particular, Aebersold et al. exemplify adding a labeling reagent to a complex protein mixture, which is then cleaved into peptide fragments; peptide fragments that are labeled are then isolated and identified (ibid). By isolating and analyzing the isolated peptide fragments, the presence of protein(s) in the sample can be determined since the peptides are characteristic of the originating protein (column 3, lines 39-68). For example, sequence identification of multiple peptide components of a protein mixture can be obtained in a single analysis (see also heading to Table 2). Since the resulting peptide fragments are characteristic of the presence of the protein from which they originated, isolation and characterization of the peptide fragments can be used to determine the presence of the protein in the complex mixture (see also the abstract).

As discussed above, the affinity labeling reagent of Aebersold et al. (which may react with sulfhydryl groups) is highly analogous to the iodoacetic acid modifying reagents of Creighton et al., which may also be sulfhydryl reactive.

Therefore, when performing the method of Creighton in order to analyze complex samples such as blood, cells or tissue (as taught by Aebersold et al.), it would have been obvious to treat the samples with a protease as taught by Aebersold et al. (thereby cleaving proteins therein to form a protein peptide mixture) as a necessary step prior to analysis by mass spectrometry. In particular, one would be motivated to digest the sample into peptide fragments so that the presence of the protein from which the fragments originated could be identified. Although Creighton exemplifies labeling a mixture of peptides, it would have been obvious to

first label the complex mixtures of proteins (e.g., blood, cells, tissue) taught by Aebersold with the labeling compound of Creighton and to subsequently digest the sample into a protein-peptide mixture because this order is exemplified in the analogous methods of Aebersold et al. In addition, the selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results. See MPEP 2144.04.

Motivation to combine the reference teachings in this manner also comes from the teachings of Creighton, since the diagonal chromatography procedures are performed on mixtures of peptides.

With respect to claims 5-7, Aebersold et al. teach that isolated peptides can be characterized by mass spectrometric techniques: in particular, the sequence of isolated peptides can be determined using mass spectrometry techniques, and by application of sequence database searching techniques, the protein from which the sequenced peptide can be identified using the mass spectrometry data (which measures the peptide masses). See column 3, lines 54-60; and columns 13-14.

Therefore, when performing the peptide isolation method of Creighton on a complex protein mixture in order to identify proteins in the mixture (as taught by Aebersold et al.), it would have been further obvious to one of ordinary skill in the art at the time of the instant invention to identify the isolated peptides by mass spectrometry in combination with sequence database searching as taught by Aebersold et al. because Aebersold et al. taught that isolated peptides can be sequenced and characterized by mass spectrometry in this manner, thereby allowing identification of the protein from which they originate, and consequently allowing for determination of the presence of that protein in the complex mixture.

19. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Creighton in view of Aebersold et al. as applied to claim 1 above, and further in view of the evidence of Sahasrabudhe (U.S. 5,705,351) or Chang (U.S. 5,474,780).

Creighton is as discussed above, which teaches compounds including fluoro-2,4,-dinitrobenzene and maleic anhydride to modify specific amino acid residues (see especially page 41, right column; page 31, right column; and page 11, left column). However, the reference is silent as to whether such compounds are drugs.

Sahasrabudhe provides evidence that fluoro-2,4-dinitrobenzene is a drug[1] in that it can be used to chemically treat cells for therapy of non-leukemic cancer (column 3, line 34 to column 4, line 16; column 17, lines 29-49). In addition, fluoro-2,4-dinitrobenzene can be used in diagnosis, e.g. to identify patients at risk of cancer or to monitor therapy in cancer patients (column 7, line 31 to column 8, line 2; column 14, line 31 to column 15, line 28).

Chang teaches that maleic anhydride is used as an ingredient in medical preparations for drug delivery (abstract and column 3, lines 1-21).

Therefore, in light of the evidence of Sahasrabudhe and Chang, the teachings of Creighton and Aebersold et al. meet the claim as the compounds taught by Creighton are drugs.

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[1] A "drug" is defined in the art as "a substance intended for use in the diagnosis, cure, treatment, or prevention of disease"; "a substance that has a particular effect on the body" (Penguin English Dictionary); "any substance used as an ingredient in medical preparations"; "any substance that affects the normal body functions" (Collins Dictionary of Biology).

20. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Creighton in view of Aebersold et al. as applied to claim 1 above, and further in view of GE Healthcare ("Fraction Collectors: Frac-950 and Frac-920", Data File 18-1153-57 AD (May 2001), retrieved from http://www1.gelifesciences.com on 4/8/09).

Creighton and Aebersold et al. are as discussed above. Creighton teaches HPLC chromatography but fails to provide details regarding the specific procedures to be used. Therefore, the references fail to specifically teach pooling fractions to avoid elution overlap between different peaks.

However, it was known in the art to adjust the size of collected fractions when performing chromatographic procedures in order to avoid re-mixing of proteins separated on the column. See GE Healthcare at column 3, "Collect the fractions you want", where it is discussed that while too many fractions will make for too much work (many tubes), while a fraction size that is too large will result in loss of resolution as peaks separated on the column will be re-mixed in the collected fractions. GE Healthcare teaches that by using automated peak fractionation, peak overlap can be reduced (Figure 7).

Therefore, it would have been obvious to one of ordinary skill in the art to employ automated peak fractionation, thereby pooling fractions in such a way as to reduce peak overlap, because GE Healthcare taught that such procedures achieve the best results in chromatography (which is the technique employed by Creighton).

Response to Arguments

21. Applicant's arguments, filed 12/22/08, have been fully considered.

22. With respect to the rejections of claims 2-3 and 5-7 under § 103 as being unpatentable over Creighton in view of Aebersold, Applicant's arguments (Reply, pages 12-22) have been fully considered but are not found persuasive.

Applicant argues that one would not have been motivated to combine the diagonal techniques of Creighton with Aebersold's mass spectrometry-based analysis of complex mixtures of proteins (Reply, paragraph bridging pages 20-21), to which the Examiner disagrees for reasons of record as set forth above. In particular, the methods of Creighton and Aebersold are highly analogous in that each teaches methods to isolate specific peptides from mixtures by selective labeling procedures.

Applicant agues that Creighton does not relate to isolation of specific interaction partners of a compound (Reply, page 21, first full paragraph). This is not found persuasive because the compounds taught by Creighton are specific for specific amino acid groups in peptides. Therefore, the compounds specifically interact with certain peptides, i.e. those containing the reactive amino acids. As such, the methods of Creighton isolate specific reactive peptides that would be considered "specific interaction partners" when this terminology is given its broadest reasonable interpretation.

Applicant further argues that Creighton does not teach complex mixtures (Reply, page 21, first full paragraph). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA

1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Although it is acknowledged that the reference does not teach complex mixtures *containing 100 or more different molecules*, the Aebersold reference has been relied upon for this teaching.

Applicant further argues that Creighton fails to disclose a compound having a specificity-determining part in addition to a linking and alteration part (Reply, page 21, first full paragraph). This is not found persuasive because it is evident that the compounds taught by Creighton specifically interact with certain amino acids. As such, the compounds may be said to possess chemical structures that determine the specific interactions with these amino acids. In addition, the compounds also possess functional groups that can be altered, as for example by detachment of the compounds from the amino acids.

Applicant further argues that Aebersold does not relate to interaction partner isolation (page 21, third paragraph), to which the Examiner disagrees. As in Creighton, the methods of Aebersold also result in the isolation of those peptides in a mixture that specifically react with compound (affinity labeled protein reactive reagent). See, e.g., the abstract and column 4, lines 26-39.

Applicant further argues that Aebersold et al. teaches away from the claimed invention in stressing that every protein should be ideally represented by at least one peptide (Reply, paragraph bridging pages 21-22). This is not found persuasive because Applicant has not pointed to any claim language that would serve to distinguish the claimed invention on this basis.

Conclusion

Claims 1-7 and 13-14 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached at (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine Foster/
Examiner, Art Unit 1641

/Christopher L. Chin/
Primary Examiner, Art Unit 1641